

Telaprevir (*Incivek*)

Discontinued. This treatment has been discontinued.

Table of Contents

- [Telaprevir *Incivek* Summary](#)
- [Drug Summary](#)
- [Adverse Effects](#)
- [Class and Mechanism](#)
- [Manufacturer for United States](#)
- [FDA Status](#)
- [Indications](#)
- [Dosing](#)
- [Clinical Use](#)
- [Cost and Medication Access](#)
- [Resistance](#)
- [Key Drug Interactions](#)
- [Full Prescribing Information](#)
- [Figures](#)

Drug Summary

Although telaprevir was a promising direct-acting antiviral agent that had impact in the hepatitis C treatment field during 2011 to 2013, it was subsequently replaced by newer direct-acting antiviral agents that were more effective, better tolerated, and more convenient. Based on the dwindling role of telaprevir after newer direct-acting antiviral agents were approved, Vertex pharmaceuticals discontinued the sales and distribution of telaprevir in the United States in October 2014. Telaprevir does have some current importance since persons who previously failed a telaprevir-based regimen may have developed resistant associated variants, which could potentially impact subsequent therapy.

Adverse Effects

The most significant adverse effects reported in the main registration trials and in post-marketing experience were rash, anorectal complaints, and anemia. When comparing triple therapy of telaprevir, peginterferon, and ribavirin with dual therapy of peginterferon and ribavirin alone significant differences were noted with rash (56% versus 34%), anemia (36% versus 17%), and anorectal complaints that include anorectal discomfort, anal pruritus, and hemorrhoids (29% versus 7%). In most cases, the rash that develops is eczematous or maculopapular in character and mild to moderate in severity; the rash is typically manageable with good skin care and topical emollients or corticosteroids. In some instances, however, telaprevir has caused serious skin

rashes, including Steven's Johnson Syndrome (SJS), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), and Toxic Epidermal Necrolysis (TEN). Telaprevir has a black box warning for fatal and non-fatal serious skin reactions.

Class and Mechanism

Telaprevir (*Incivek*) is a NS3/4A hepatitis C protease inhibitor. Specifically, telaprevir inhibits the proteolytic cleavage of the HCV encoded polyprotein, an essential step in the viral life cycle for the production of mature forms of the viral proteins NS4A, NS4B, NS5A, and NS5B.

Manufacturer for United States

Telaprevir (*Incivek*) is no longer manufactured in the United States. Telaprevir ([Figure 1](#)) was previously manufactured by Vertex Pharmaceuticals. Vertex pharmaceuticals discontinued the sales and distribution of telaprevir in the United States in October 2014, primarily due to available alternative treatments and diminishing market demands. The drug telaprevir was formerly known as VX-950 and was co-developed by Vertex Pharmaceuticals and Johnson & Johnson.

FDA Status

Telaprevir was approved by the U.S. FDA on May 23, 2011 for the treatment of adults with chronic hepatitis C. Telaprevir (*Incivek*) is no longer manufactured in the United States.

Indications

The following list summarizes the key points related to telaprevir indications.

- Telaprevir is approved for use in combination with peginterferon and ribavirin to treat adults with genotype 1 chronic hepatitis C infection and compensated liver disease.
 - Telaprevir is approved for hepatitis C treatment-naïve patients and patients with prior interferon-based treatment, including null responders, partial responders, and relapsers.
 - Telaprevir should never be used as monotherapy due to the rapid development of resistance when used alone.
 - A high percentage of treatment-experienced patients who had a prior null response do not obtain an SVR when treated with a telaprevir-based regimen.
 - The efficacy of telaprevir in patients who have previously failed a regimen that included a protease inhibitor is unknown.
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Dosing

Telaprevir was available in 375 mg tablets ([Figure 2](#)). The recommended telaprevir dosing is 1125 mg (three 375 mg tablets) taken twice daily with food (not low fat); dosing every 10 to 14 hours is considered acceptable and ideally the food meal should contain at least 20 grams of fat for optimal absorption of the drug. No dose adjustment is recommended for patients with mild, moderate, or severe renal impairment; telaprevir has not been studied in patients on hemodialysis. The dose of telaprevir does not need adjusting in patients with mild hepatic impairment (Child-Pugh A); telaprevir is not recommended for use in patients with severe hepatic impairment (Child-Pugh B or C).

Clinical Use

The following summarizes how telaprevir was used. Telaprevir is given with peginterferon and ribavirin for the first 12 weeks of therapy, followed by an additional 12 or 36 weeks of peginterferon and ribavirin dependent on the response during therapy and the patient's prior treatment response status.

- Response-guided therapy is used for treatment-naïve patients and treatment-experienced patients with prior relapse. If HCV RNA levels are undetectable at weeks 4 and 12 of therapy, the patient should receive an additional 12 weeks of peginterferon and ribavirin (total duration of telaprevir 12 weeks and peginterferon and ribavirin 24 weeks). If the HCV RNA levels is detectable at a low level (1000 IU/mL or less) at week 4 and undetectable at week 12 of therapy, the patient should receive an additional 36 weeks of peginterferon and ribavirin (total duration of telaprevir 12 weeks and peginterferon and ribavirin for 48 weeks).
 - Treatment-experienced patients with prior partial response or null response should receive an additional 36 weeks of peginterferon and ribavirin (total duration of telaprevir 12 weeks and peginterferon and ribavirin 48 weeks).
 - For treatment-naïve patients with cirrhosis most experts recommend using an additional 36 weeks of peginterferon and ribavirin (total duration of telaprevir 12 weeks and peginterferon and ribavirin 48 weeks), even if HCV RNA levels are undetectable at weeks 4 and 12 of therapy.
 - For any patient on a telaprevir-based regimen, therapy should be discontinued if: (a) the patient has an HCV RNA level greater than 1000 IU/mL at week 4 or 12, or (b) the patient has a detectable HCV RNA level at week 24.
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Cost and Medication Access

In 2014, Vertex Pharmaceuticals discontinued its sales of telaprevir in the United States.

Resistance

Treatment-emergent resistance mutations (NS3 amino acid substitutions conferring reduced susceptibility to telaprevir) were common among subjects in phase 3 trials who did not achieve SVR. In pooled analysis of the 525 subjects who did not achieve an SVR, 62% developed treatment-emergent variants – this occurred more

frequently in genotype 1A patients (69%) than 1B patients (45%), and was observed in nearly all patients who failed telaprevir-based therapy during the first 12 weeks. The most common mutations to develop were V36M/A/L, T54A/S, R155K/T, and A156S/T; these mutations may develop alone or as combinations of mutations.

Key Drug Interactions

Telaprevir is a strong inhibitor of cytochrome p450 3A4 (CYP3A) and can also inhibit p-glycoprotein (P-gp), OATP1B1, and OATP2B1. Accordingly, when used concomitantly, telaprevir can have a significant impact on plasma concentrations of drugs that are metabolized by CYP3A, P-gp, OATP1B1, or OATP2B1. In addition, telaprevir is primarily metabolized by CYP3A. The coadministration of telaprevir with drugs that induce or inhibit CYP3A4/5 could decrease or increase telaprevir levels. See the [Telaprevir \(Incivek\) Full Prescribing Information](#) for a detailed description of important drug interactions with telaprevir. For complete information on telaprevir-related drug interactions, see the [Drug Interactions section in the Telaprevir \(Incivek\) Prescribing Information](#).

Full Prescribing Information

[Telaprevir \(Incivek\) Full Prescribing Information](#). Note that telaprevir is no longer manufactured in the United States.

Figures

[Figure 1. Telaprevir \(Incivek\) Box](#)

Photo: Andrew Karpenko, University of Washington

[Figure 2. Telaprevir \(Incivek\) Tablet](#)

Photo: Andrew Karpenko, University of Washington

